preliminary results from an IRB-approved prospective, open label, phase II trial to test the efficacy of montelukast, a leukotriene inhibitor, for the treatment of BOS after HSCT. BOS diagnostic criteria included: FEV1 < 75%, FEV1/VC < 0.7 or air trapping on CT and RV > 120% or RV/TLC > 120% in the absence of infection and presence of another cGVHD manifestation. Eleven patients have enrolled to date. One withdrew prior to medication initiation and 9/10 are currently on study medication (10 mg montelukast po nightly). Patient characteristics include age range 15-60 years, 7/11 female, baseline FEV1 range from 33 to 71% predicted, and 3/11 patients requiring oxygen supplementation. Sixty-four % (7/11) have reached the primary endpoint (6 months of study drug). FEV1 increased by 6-10% predicted in 3 patients, remained stable in 3, and declined by less than 15% in 1. Slope of the FEV1 value generated as linear regression of FEV1 volume vs. days post-transplant revealed: 5/7 increase in slope, 2/7 decrease in slope from pre-study FEV1 values. Three patients had immunosuppression reduced during this time period with complete cessation of tacrolimus in 1, cessation of steroids in 1, and decreased tacrolimus in 1(including 2 with stable FEV1 and 1 with increase in FEV1); 1 patient had an increase in steroid dose less than 1 mg/kg/day. Two patients had worsening of other cGVHD manifestations on study, including a skin flare that resolved without increasing systemic therapy (1) and gastrointestinal cGVHD flare that improved with increased steroids including local therapy (1). Montelukast was well-tolerated with one grade II attributable adverse event (insomnia) during the six-month collection period. Improvements were also noted in oral mucosa cGVHD manifestations in 3/7 and liver in 2/7. These preliminary findings suggest that montelukast may have a role in the therapy of BOS after allogeneic HSCT.

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POMALIDOMIDE (POM) IN ADVANCED CORTICOSTEROID-RESISTANT CHRONIC GRAFT-VERSUS-HOST DISEASE (CGVHD)

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Background: Thalidomide is active in cGVHD, but with troublesome side effects such as neutropenia, neuropathy and somnolence. POM is a member of the new class of immune-modulating drugs (IMiD®) >100-fold more potent than thalidomide in inhibiting production of TNFα and increasing Th1-cells. We assessed efficacy and safety of POM in people with corticosteroid-resistant cGVHD.

Methods: Subjects had to have moderate (N = 2) or severe (N = 6) cGVHD (NIH criteria), and failed prednisone (0.5 mg/kg/d for >8 w) and/or 2nd-line immune-suppression. No ECP in the preceding 3 m or new therapy in the preceding 1 m was allowed. POM was given by mouth at a starting dose of 3 mg/d with dose-reduction to 2, 1, and 0.5 mg/d for intolerance or adverse events. Subjects were evaluated for response every 3 m. Responses were assessed based upon changes in signs or symptoms of each organ system and overall response was than determined using NIH Criteria.

Results: 8 subjects are enrolled so far. Median time posttransplant is 2.9 y (1.5-6 y), median time since diagnosis of cGVHD is 1.8 y (1-4.5 y), 4 subjects received related- and 4 unrelated-allotransplants; 5 had prior acute GVHD. Median N of prior systemic cGVHD therapies was 3 (2-5). Affected organs included skin (N = 8), mouth (N = 8), eye (N = 7), GI (N = 5), musculo-skeletal (N = 4), liver (N = 2), genital (N = 2) and lung (N = 2). Median KPS was 80%. 7 subjects required dose-reductions for muscle cramps, tremors and/or fatigue. There was no bone marrow suppression, neuropathy, somnolence or thrombosis. 5 subjects discontinued therapy: 1 for worsening skin and mouth lesions, 3 for no response (2 had worsening tremors, muscle cramps and fatigue) and 1 for worsening pain. 1 subject died of a heart attack 4 m after stopping POM. 3 subjects completed 6 m of therapy and underwent 2nd response evaluation: 2 at 2 mg/d and 1 at 1 mg/d. 2 have a complete response (CR) and 1 a partial response (PR) of erythematous skin changes and a CR of GI symptoms. There are ongoing improvements <PR in skin, mouth, and eyes. 3 subjects have a global PR.

Conclusion: POM can be given for corticosteroid-resistant cGVHD without toxicities that limit use of thalidomide in this context. Our data suggest POM is active in moderate/severe corticosteroid-resistant cGVHD. 3 mg/d is likely a too high starting dose: we recommend 1-2 mg/d in future studies. Subject accrual continues, as do correlative laboratory studies; these data will be reported.

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A PROSPECTIVE STUDY OF DONOR IMMUKNOW® AS A BIOMARKER FOR ACUTE GVHD IN HEMATOPOIETIC CELL TRANSPLANTATION RECIPIENTS

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Introduction: Graft versus host disease (GvHD) occurs in ~40% of allogeneic hematopoietic cell transplantation (HCT) recipients and is associated with substantial morbidity and mortality. Immunological parameters of donor cells that predispose a recipient to GvHD will be of great value. The Cylex™ ImmuKnow® assay determines the strength of immune function by quantifying the amount of ATP released from phytohemagglutinin-stimulated peripheral blood $CD4^+$ cells. In our current study, we utilized the ImmuKnow® to assess whether a donor's immune response correlates with early outcomes in recipients post-HCT.

Patients and Methods: Twenty-six (26) donor-recipient pairs were included in our study (15 HLA identical sibling HCT and 11 haploidentical HCT). Recipients received an average cell-dose of $10.7 \pm 4.9 \times 10^6$ $CD34^+$ cells/kg. Blood samples obtained prior to G-CSF mobilization and prior to stem cell collection (approximately 2 weeks apart) were assayed for ImmuKnow values and cell counts (WBC, ANC, ALC & $CD34^+$ count).

Results: G-CSF mobilization led to a significant increase in ImmuKnow® ATP values from 342 to 728 ng/mL ($p < 0.001$) along with an increase in all measured cell counts. Grade ≥ II acute GvHD occurred in 27% of haploidentical HCT recipients (3/11 patients) and 20% of HLA identical HCT recipients (3/15 patients). In haploidentical HCT, mobilized donor blood ImmuKnow® ATP values did not correlate with GvHD. However, donor ImmuKnow® values correlated with increased risk of acute GvHD in HLA identical sibling HCT. In HLA identical sibling HCT, ATP values in excess of 747 ng/mL predicted grade II or higher GvHD with a likelihood ratio of 4.00 (2.9-5.5, 95% confidence), sensitivity of 100%, and specificity of 75% (AUC = 0.889, $p = 0.003$).

Conclusions: If confirmed in larger studies, these data suggest that ImmuKnow can serve as an independent predictor/biomarker for the development of GvHD in HLA identical HCT.

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MYCOPHENOLATE MOFETIL AS THERAPY FOR STEROID DEPENDENT OR REFRACTORY GRAFT VERSUS HOST DISEASE: TEN YEARS EXPERIENCE FROM A SINGLE CENTER IN BRAZIL

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Chronic graft-versus-Host-Disease (GVHD) is observed in up to 50% of long term survivors of hematopoietic stem cell transplants (HSCT) and is associated to important morbidity and mortality. Mycophenolate Mofetil (MMF) has been used as therapy for refractory chronic GVHD with good efficacy and tolerability. We describe our experience at Hospital de clínicas of Federal University of Paraná-Brazil during the last ten years on the use of this drug as rescue for refractory chronic GVHD.